A & G PHARMACEUTICALS, INC.
P.O. BOX 365
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September 8, 1999.

Dr. Lonnie Luther
Quality Assurance Support Team (HFV-102) Room 387
FDA Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855

Dear Dr. Luther,

Please find enclosed a suitability petition submitted on behalf of A & G Pharmaceuticals of Clarksburg, NJ 08510. A & G requests consideration of this suitability petition to file an ANADA for Phenylbutazone Powder for horses.

Please call if you have questions.

Sincerely,

George Green
President

99P-4167

CP1

SUITABILITY PETITION

IDENTIFICATION OF PETITIONER:

This Suitability Petition is submitted on behalf of A & G Pharmaceuticals, Clarksburg, NJ 08510 under Section 512 (n)(3) of the Federal Food, Drug, and Cosmetic Act.

ACTION REQUESTED:

The petitioner requests permission from the Commissioner to file an Abbreviated New Animal Drug Application (ANADA) for a different dosage form of an approved pioneer product. The pioneer product is Phoenix Scientific Inc. PHENYLBUTE™ (Phenylbutazone Tablets, USP), approved by the Food and Drug Administration under NADA 91-818. A copy of the pioneer product labeling (package insert) is provided (Attachment 1).

The ANADA will provide for the use of a flavored powder dosage form for administration in the grain ration for horses rather than the tablet form of the pioneer product. Both.the proposed and the pioneer products are delivered orally. The active ingredient (phenylbutazone) will be formulated to contain 1 g phenylbutazone per 10 grams of a palatable powder. The pioneer product is formulated to contain 1 gram of phenylbutazone per tablet. Both the proposed and pioneer products are provided to affected animals at the rate of 2-4 mg phenylbutazone per pound of body weight.

The product labeling will provide for indications, recommended dosages, contraindications, precautions and warnings identical to the pioneer product. Draft labeling for the proposed product is provided (Attachment II).

The proposed product label differs from the pioneer product specifically as follows:

1. Labeled as “Powder” rather than “Tablet”.

2. Contents are labeled as phenylbutazone per 10 grams of powder rather than per tablet.

3. The **Dosage and Administration** instructions are revised to describe delivery of the powder drug product (using a measuring cup provided) mixed in the grain ration.

4. It is anticipated that stability studies will support storage at room temperature conditions.

5. The net contents of the containers are yet to be determined.

STATEMENT OF GROUNDS:

The proposed product contains the same active ingredient and will be labeled with the same indications, recommended dose rates, contraindications, precautions and warnings **as** the approved pioneer product. Because of oral administration and absorption after the phenylbutazone is dissolved in the stomach, the clinical effect for both drugs is expected to be similar. The sponsor intends to provide results of blood level bioequivalency testing to demonstrate efficacy and safety of the product as well as palatability information for the product.

ENVIRONMENTAL IMPACT:

The action of submitting this Suitability Petition and its review by the FDA - Center for Veterinary Medicine is not expected to have an environmental impact. The action requested qualifles for categorical exclusion under 21 CFR Part 25.30(h) from the requirement for an environmental assessment and, to the best of the sponsor's knowledge, no extraordinary circumstances exist.

ECONOMIC IMPACT:

An "Economic Impact" analysis of this action will be provided if requested by the Commissioner.

CERTIFICATION:

A & G Pharmaceuticals certifies that this suitability petition contains all information known to them which is unfavorable to the petition.

9/8/99

George Green
President
A & G Pharmaceuticals, Inc.
P.O. Box 365 Clarksburg, NJ 08510

Attachments

1. Pioneer Product Label
2. Proposed Product Label

ATTACHMENT 1

SEE PACKAGE INSERT FOR COMPLETE **INSTRUCTIONS.**

INDICATIONS: **Phenylbutazone is for the relief of inflammatory conditions associated with the musculoskeletal system in horses.**

DOSAGE AND ADMINISTRATION: For **Horses** only: **Orally 1 to 2 tablets per 500 pounds of body weight, but not to exceed 4 g per animal daily. Use high dose for the first 48 hours, the" gradually reduce to a maintenance dose.**

801021 Iss. 2-99

Phenylbutazone Tablets, USP

1 gram

ANTI-INFLAMMATORY

FOR ORAL USE IN HORSES ONLY

KEEP OUT OF REACH OF CHILDREN

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

NET CONTENTS: 100 TABLETS

NADA 91-818, APPROVED BY FDA

Manufactured for:

A&G Pharmaceuticals

Clarksburg, NJ 08510

Each tablet contains:

Phenylbutazone . . . . . 1 gram

Dispense in tight, child resistant containers.

WARNING: Not for use in horses intended for food.

Store at controlled **room temperature, 20°** to **25°C (68°** to **77°F)**

Manufactured by
Phoenix Scientific, Inc.
St. Joseph, MO 64503

Cot No. **Exp. Date**

Sample

PHENYLBUTAZONE TABLETS, USP 1 gram

AM/BT/AG/BI

NADA 91-818, Approved by FDA

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Phenylbutazone chemically is 4-butyl-1, 2 diphenyl-3, 5-pyrazolidinedione.

$C_{19}H_{20}N_2O_2$

Mol. Wt. 308.38

Each tablet contains 1 g of phenylbutazone

BACKGROUND PHARMACOLOGY: Phenylbutazone was first synthesized in 1948 and introduced into human medicine in 1949. Kuzell (1), (2), (3), Payne, (4), Fleming, (5) and Denko, (6) demonstrated the clinical effectiveness of phenylbutazone in gout, gouty arthritis, acute arthritis, acute rheumatism and various other rheumatoid disorders in humans. Fabre (7), Domenjoz, (8), Wilhelmi, (9) and Yourish, (10), have established the anti-rheumatic and anti-inflammatory activity of phenylbutazone. It is entirely unrelated to the steroid hormones.

Toxicity of phenylbutazone has been investigated in rats and mice (11), and dogs (12).

Phenylbutazone has been used by Camberos (13), in thoroughbred horses. Favorable results were reported in cases of traumatism, muscle rupture, strains and inflammations of the third phalanx. Results were not as favorable in the periodic treatment of osteo-arthritis of the stifle and hip, arthrosis of the trapezious muscles and general arthritis. Sutter, (14) reported a favorable response in chronic equine arthritis of long duration, fair results in severely bruised mare and poor results in two cases where the condition was limited to the third phalanx.

INDICATIONS: Phenylbutazone is for the relief of inflammatory conditions associated with the musculoskeletal system in horses.

DOSAGE AND ADMINISTRATION: For Horses Only: Orally 1 to 2 tablets per 500 pounds of body weight, but not to exceed 4 g per animal daily. Use high dose for the first 48 hours, then gradually reduce to a maintenance dose.

CONTRAINDICATIONS: Use with caution in patients who have history of drug allergy.

PRECAUTION: In the treatment of inflammatory conditions associated with infections, specific anti-infective therapy should be used concurrently.

WARNING: Not for horses intended for food.

HOW SUPPLIED: Tablets containing 1 gram of phenylbutazone are supplied in bottles of 100 tablets.

Store at controlled room temperature, 20' to 25°C (68' to 77°F)

References:

1. Kuzell, WC, Schaffarzick, RW, Naughler, WE, Gandia, C and Mankle, EA: A.M.A. Arch. Inst. Med., 92,646 (1953).
2. Kuzell, WC, Schaffarzick, RW, Brown, B and Mankle, EA: J.A.M.A. 149; 729 (1952).
3. Kuzell, WC, and Schaffarzick, RW: Calif. Med. 77; 319 (1952).
4. Payne, RW, Shelter, MR, Farr, CH, Hellbaum, AA, and Ishmall, WK: J. Lab. Clin. Med. 45; 331 (1955).
5. Fleming, J and Will, G: Ann. Rheumat., Dis., 12; 95 (1953).
6. Denko, CW and Rumi, D: American Pract. 6; 1865 (1955).
7. Fabre, J, et al: Semain. Hop. (Paris) 31; 87 (1955).
8. Domenjoz, R, et al: Arzneimittel-Forsch, 5; 488 (1955).
9. Wilhelmi, G and Pulver, R: Arzneimittel-Forsch, 5; 221 (1955).
10. Yourish, W, Paton, B, Brodie, B, Burns, J: A.M.A. Arch. Ophth., 53: 264 (1955).
11. Hazelton, LW, Tusing, TW and Hollana, EG: J. Pharmacol, Exper. Ther., 109; 387 (1953).
12. Ogilvie, FB and Sutter, MD: Vet. Med 52; 492-4 (1957).
13. Camberos, HR: Rev. Med. Vet. (Buenos Aries) 38: 9 (1956).
14. Sutter, MD: Vet. Med., 53; 83 (Feb. 1958).
15. Gabriel, KL, Martin, JE: J. Am. Vet. Med. A. 140; 334-41 (Feb. 1962).

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Rev. 3/99

Manufactured by
Phoenix Scientific, Inc.
St. Joseph, MO 64503

ATTACHMENT 2

Phenylbutazone Powder

ANADA XXX-XXX, Approved by FDA

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Phenylbutazone chemically is 4-butyl-1,2-diphenyl-3,5-pyrazolidinedione.

$C_{19}H_{20}N_2O_2$

Mol. Wt. 308.38

Each 10 g contains 1 g phenylbutazone

BACKGROUND PHARMACOLOGY: Phenylbutazone was first synthesized in 1948 and introduced into human medicine in 1948. Kuzell (1), (2), (3), Payne, (4), Fleming, (5) and Denko, (6) demonstrated the clinical effectiveness of phenylbutazone in gout, gouty arthritis, acute arthritis, acute rheumatism and various other rheumatoid disorders in humans. Fabre (7), Domenjoz, (8), Wilhelmi, (9) and Yourish, (10), have established the anti-rheumatic and anti-inflammatory activity of phenylbutazone. It is entirely unrelated to the steroid hormones.

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INDICATIONS: Phenylbutazone is for the relief of inflammatory conditions associated with the musculoskeletal system in horses.

DOSAGE AND ADMINISTRATION: For Horses Only: Administer on a small amount of palatable feed 10 to 20 grams of powder (1 or 2 tablespoons in the measuring cup provided) per 500 pounds of body weight, but not to exceed 4 g per animal daily. Use high dose for the first 48 hours, then gradually reduce to a maintenance dose.

CONTRAINDICATIONS: Use with caution in patients who have history of drug allergy.

PRECAUTION: In the treatment of inflammatory conditions associated with infections, specific anti-infective therapy should be used concurrently.

WARNING: Not for horses intended for food.

HOW SUPPLIED: Powder containing 1 gram of phenylbutazone per 10 grams of powder are supplied in 2.2 lbs. ***(Net contents of containers are to be determined).***

Store at controlled room temperature, 20E to 25E C (68E to 77E F). *(It is anticipated that*

stability* data will *support this storage labeling).

References:

1. Kuzell, WC, Schaffarzick, RW, Naughler, WE, Gandia, C and Mankle, EA: A.M.A. Arch. Inst. Med., 92,646 (1953).
2. Kuzell, WC, Schaffarzick, RW, Brown, B and Mankle, EA: J.A.M.A. 149; 729 (1952).
3. Kuzell, WC, and Schaffazick, RW: Calif. Med. 77; 319 (1952).
4. Payne, RW, Shelter, MR, Fan, CH, Hdlbaum, AA, and Ishmall, WK: J. Lab. Clin. Med. 45; 331 (1955).
5. Fleming, J and Will, G: Ann. Rheumat., Dis., 12; 95 (1953).
6. Denko, CW and Rumi, D: American Pract. 6; 1865 (1955).
7. Fabre, J, et al: Semain. Hop. (Paris) 31; 87 (1955).
8. Domenjoz, R, et al: Arzneimittel-Forsch, 5; 488 (1955).
9. Wilhelmi, G and Pulver, R: Arzneimittel-Forsch, 5; 221 (1955).
10. Yourish, W, Paton, B, Brodie, B, Burns, J: A.M.A. Arch. Ophth., 53:264 (1955).
11. Hazelton, LW, Tusing, TW and Hollana, EG: J. Pharmacol, Exper. Ther., 109; 387 (1953).
12. Ogilvie, FB and Sutter, MD: Vet. Med 52; 4924 (1957).
13. Camberos, HR: Rev. Med. Vet. (Buenos Aries) 38: 9 (1956).
14. Sutter, MD: Vet. Med., 53; 83 (Feb.1 958).
15. Gabriel, KL, Martin, JE: J. Am. Vet. Med. A. 140; 334-41 (Feb. 1962).

Manufactured for A & G Pharmaceuticals Inc., Clarksburg, NJ 08510

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